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Division of Dockets Management (HFA-305)
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Opposition To Pfizer Petition Seeking To Block FDA's Lawful Approval Of Omnitrope®
Docket No. 2004P-0231/CP1

Faced with the prospect of lawful competition to its decade-old Genotropin product, Pfizer has launched a frenzied initiative to preserve the unpatented, "legacy" franchise it purchased from Pharmacia by attempting to arrest the progress of the scientific review of Sandoz's confidential new drug application ("NDA") for approval of Omnitrope via a last-minute petition to the Food and Drug Administration ("FDA"). Although replete with legal and scientific flaws, Pfizer's petition suffers from more basic and egregious errors. Specifically, the petition (i) improperly places on the public record Sandoz's valuable and proprietary drug development information embodied in a draft Sandoz protocol in violation of Pfizer's own policies on the confidentiality of study protocols, and (ii) mistakenly bases its most serious objections on a passage of that draft protocol, which clearly contains a significant typographical error that goes to the heart of Pfizer's scientific case. See CP1, vol. II, Ex. 4.

Putting aside for the moment Pfizer's unclean hands resulting from its misuse of the type of proprietary information that Pfizer incorrectly accuses FDA of misappropriating, Pfizer has seized upon a conspicuous misprint in that internal Sandoz draft protocol (subsequently corrected) relating to what Pfizer asserts is a difference in the molecular weight of 1,001 daltons between its "legacy" Genotropin product and Sandoz's Omnitrope. Indeed, Pfizer has elevated that typo to make it the raison d'être of its global strategy to interfere with approval of Sandoz's lawfully competing product. Having engaged a virtual army of lawyers to represent Pfizer before the U.S. FDA,[1] but apparently lacking a copy of the final version of the protocol, Pfizer and its lawyers have proceeded to make that basic scientific error the linchpin of their strategy to preclude approval of Omnitrope. In light of the fact that Genotropin already is the subject of an

[1] Four lawyers from an outside law firm and three in-house Pfizer lawyers have allowed their names to appear on the instant petition, all of whom jointly share responsibility with the corporation for the factual allegations and legal arguments presented in the petition.

ongoing Justice Department investigation,[2] more thorough due diligence reasonably could have been expected, e.g., review of basic texts, consultation with Pfizer's own Senior Vice President, Science and Technology, or other scientists, or even contacting Sandoz. Regrettably, Pfizer proceeded without taking any reasonable steps, and thereby failed FDA by neglecting its duty to investigate this critical factual premise of its arguments.

It is obvious that FDA would not have accepted an NDA for filing, much less reviewed it up to this stage, for a product with a 1,001 daltons difference from Genotropin if it were represented to be human growth hormone.[3] Instead, the Agency would have, correctly, rejected such a submission out of hand. In actuality, the Agency properly has proceeded with its rigorous scientific review of Sandoz's NDA because FDA has access in its confidential files to Sandoz's trade secrets and confidential business information, which adequately demonstrates the fallacy of Pfizer's petition. Sandoz obviously has no intention of disclosing any of its proprietary information here – Pfizer has disclosed enough already. Nonetheless, Sandoz is confident that the Agency can continue and complete its thorough and fully-informed, science-based review of Sandoz's confidential NDA without being distracted by the specious arguments advanced by Pfizer and its cadre of lawyers.

Toward that end, with the "factual" foundation pulled out from under the argument constructed by Pfizer, and in light of the numerous other fundamental flaws in Pfizer's legal and scientific argumentation, the Agency should deny Pfizer's petition forthwith. Summary dismissal also is uniquely appropriate here given Pfizer's prior, written acceptance of the Agency's longstanding policy on Section 505(b)(2), which Pfizer has failed to disclose in the myriad of legal proceedings Pfizer has initiated against the Agency. See CP1 at 2 n.3. Accordingly, for the reasons set forth below, the Agency should dismiss Pfizer's filing in this docket for what it is: an attempt to prevent Sandoz from engaging in legitimate competition.

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[2] Pfizer, Inc., 10-K For Fiscal Year 2003, U.S. SEC (filed Mar. 10, 2004), Exhibit 13, 2003 Financial Report, at 50 ("The Company recently was notified that the U.S. Department of Justice is conducting investigations relating to the marketing and sale of *Genotropin* and *Bextra*, as well as certain managed care payments."), excerpt attached as Ex. 1. Recent events would suggest that, should DoJ's ongoing Genotropin investigation trigger criminal and/or civil charges against Pfizer, the company will attempt to deflect liability by referring to the "legacy" nature of any such charges based upon pre-acquisition conduct by a predecessor company. See, e.g., Statement on *Financial Provisions Recorded for Two Legacy Warner-Lambert Legal Matters* in "Pfizer Inc. 2003 Performance Report" (Jan. 22, 2004), available at http://www.pfizer.com/are/investors_releases/2004pr/mn_2004_0122.cfm. Clearly, however, only Pfizer's current management and their lawyers devised and signed off on the instant petition, for which they alone bear full responsibility.

[3] As any collegiate biochemist knows, a 1,001 daltons difference in molecular weight, if accurate – which it is not – would represent a decrease in content of at least seven (7) amino acids and define a different product from human growth hormone.

Background

Over the course of the past two decades, the regulatory and commercial history of the injectable recombinant human growth hormone ("rhGH") segment in the U.S. has been marked by fiercely pitched competitive battles to restrain FDA approval and market entry of competing products. Until now, those prior conflicts involved unresolved legal issues relating to the Orphan Drug Act and the enforcement and validity of patents claiming various forms of rhGH – ultimately resolved by the courts.[4] This situation had resulted in a finite rhGH segment in the U.S. limited to 10 rhGH product lines, only eight (8) of which are currently marketed, produced by six (6) different manufacturers.[5] None of the products currently marketed in the U.S. has been approved on the basis of an FDA determination that it is comparable to another product currently marketed in the U.S.[6] Current IMS data indicates that the rhGH segment in the U.S. produces approximately $500 million in annual sales for these companies.

Almost 10 years ago, on August 24, 1995, FDA approved the first Genotropin application, which had been submitted by Pharmacia and Upjohn ("Pharmacia"). Pharmacia submitted its application for approval of Genotropin on May 15, 1992; the company received a "not approvable" letter two years later on May 18, 1994, and subsequently submitted 10 amendments to the application between May 1994 and August 18, 1995.[7] During the course of that 40-month review process, Pharmacia apparently was compelled to negotiate various license agreements

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[4] See, e.g., Genentech v. Bowen, 676 F. Supp. 301 (D.D.C. 1987), attached as Ex. 2; Genentech v. Novo Nordisk A/S, 108 F.3d 1361 (Fed. Cir. 1997), cert. denied, 522 U.S. 963 (1997), attached as Ex. 3. Certain rhGH patent lawsuits are still ongoing. See Novo Nordisk A/S et al.v. Bio-Technology General Corp., Ltd., et al., 2003 U.S. Dist. LEXIS 10098 (D. Del., June 9, 2003), attached as Ex. 4.

[5] Genentech (Protropin and Nutropin product lines, the first of which was approved in 1985), Lilly (Humatrope product line first approved in 1987), Novo Nordisk (Norditropin product line first approved in 1995), Pfizer (Genotropin product line first approved in 1995), Savient (Bio-Tropin and Tev-Tropin product lines, the first of which was approved in 1995), and Serono (Saizen, Serostim, and Zorbtive product lines, the first of which was approved in 1996).

[6] Outside the U.S., the rhGH segment is less stagnant. Unlike the U.S., where use of the same manufacturing processes and analytical tools that launched rhGH products almost 20 years ago is not uncommon, companies overseas have continued rhGH research and development and improved the processes for both manufacturing and delivering this important product to patients. Thus, in Germany, for example, five (5) rhGH products currently are marketed in various dosage strengths, two (2) of which originate from standard E. coli K12, two (2) of which originate from special E. coli strains, and one (1) of which is manufactured using a transformed mouse cell line. The absence of a difference between these products, and the absence of the effect of the differently constructed vectors and differently expressing host cells, has been demonstrated by highly sensitive characterization methods. The somatropin contained in all products not only has the same 191 amino acid sequence, identical with human pituitary growth hormone, but also the same potency of 3 IU per mg and the same clinical effects.

[7] *Pharmacia Genotropin Human Growth Hormone Launch Set For Early 1996*, F-D-C Reports, The Pink Sheet, 57(36): (Sep. 4, 1995), at T&G-10, attached as Ex. 5.

with the most entrenched incumbent in the rhGH segment, Genentech, in order to avoid the same resistance that had been encountered by other rhGH applications that preceded Genotropin.[8] Id. Notably, 10 years ago at the time of the Genotropin approval, Pharmacia candidly acknowledged that there was no meaningful patent protection claiming Genotropin, which, outside the U.S., had resulted in the same form of lawful competition Sandoz now seeks to initiate here:

> Although Pharmacia has some process patents relating to Genotropin, in many jurisdictions an endogenous hormone cannot be patented and several competitors have developed recombinant growth hormone products, which are available in most markets.[9]

Over the past 10 years, that situation has not changed in any meaningful way – with the exception of Sandoz' commercial decision, based upon its own trade secrets and confidential business information, to develop and seek FDA approval of a product that will compete lawfully in the U.S. rhGH segment against Genotropin. As FDA itself recognized long ago, approval of an rhGH product like Omnitrope that would compete against a product like Genotropin is a relatively straightforward matter:

> the products are non-glycosylated and highly purified and there are no isoforms; the primary structure, including disulfide bonds, has been unequivocally proven; physico-chemical tests are available for secondary and tertiary structure determination; there are clinically relevant bioassays; the mechanism of drug action is known; and there are validated biomarkers available.[10]

The Agency's longstanding scientific assessment of this well-characterized product is reinforced by the very detailed and comprehensive somatropin compendial specifications adopted by the European Pharmacopoeia and being implemented by the U.S. Pharmacopoeia.[11]

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[8] Id. See also *Bio-Technology General Bio-Tropin Preliminary Injunction Upheld*, F-D-C Reports, The Pink Sheet, 58(16): (April 15, 1996), T&G-3-T&G-4, attached as Ex. 6; *Serono Saizen Human Growth Hormone Approved With Three-Times Weekly Dosing Schedule; Somatropin Product Labeling Carries Hypothyroidism Precaution*, F-D-C Reports, The Pink Sheet, 58:42: (October 14, 1996), at 6, attached as Ex. 7.

[9] Pharmacia & Upjohn, Inc., Pre-Effective Amendment No. 2 To Form S-4, As Filed With The Securities And Exchange Commission On September 15, 1995, at 136, attached as Ex. 8.

[10] *Generic Somatropin NDAs Would Require Human Immunogenicity Tests – FDA*, F-D-C Reports, The Pink Sheet, 64(16): (Apr. 22, 2002) at 14, attached as Ex. 9.

[11] See 4 European Pharmacopoeia at 1940-1942, SOMATROPIN BULK SOLUTION Monograph No. 01/2002:0950, attached as Ex. 10; European Pharmacopoeia at 1937-1939, SOMATROPIN Monograph No. 01/2002:0951, attached as Ex. 11; 4 European Pharmacopoeia at 1942-1944, SOMATROPIN FOR INJECTION Monograph No. 01/2002:0952, attached as Ex. 12; European Directorate For The Quality Of Medicines, European Pharmacopoeia Commission, PA/PH/Exp. 6/T (03) 42 ANP, Group Of Experts No. 6 (Biological Substances), Somatropin bulk solution, Monograph N°: 950 (Dec. 2003), attached as Ex. 13; European Directorate For The

The most notable feature of the Genotropin approval – which it shares in common with all the other human growth hormone products approved by the Agency – is that it was based upon a new drug application ("NDA") under Section 505(b) of the Federal Food, Drug, and Cosmetic Act ("FD&C Act"). As a result, Genotropin (and all other rhGH products) is regulated as a drug under the FD&C Act, and all the benefits *and* liabilities of that Section 505 drug status apply.

Pfizer, like Pharmacia before it, obviously has welcomed and fully enjoyed all of the Section 505 statutory *benefits* arising from the drug status of Genotropin: non-patent data exclusivity, Orange Book patent listings, and Paragraph IV Patent Certifications like the one Sandoz provided to Pfizer.[12] Having derived its statutory benefits from the Section 505 drug status of Genotropin, Pfizer should, in the spirit of the statute, be investing in innovative new drugs that also could enjoy those benefits rather than attempting to preserve a monopoly for a 10-year-old "legacy" product.[13] Instead, Pfizer's objections have appeared just as its benefits begin to recede and the legal consequences of the status the company has enjoyed come to fruition. At this late juncture, the company is contending – contrary to well-established law and consistently applied Agency policies and practices over the past 20 years – that Genotropin is uniquely entitled to enjoy those benefits indefinitely. As set forth below, Pfizer's misplaced reliance on provisions of the FD&C Act and other statutes that have no bearing on the issues before the Agency does not alter the inescapable conclusion that this is not so.

In sum, Genotropin is not entitled to a perpetual monopoly, and Sandoz is confident that the Agency will communicate that point unequivocally by continuing its review of Omnitrope. Before it even reaches the merits of Pfizer's desperate argumentation, however, the Agency should deny the petition on the basis of Pfizer's unclean hands: there is no reason for the Agency to even entertain Pfizer's misdirected complaints about alleged misappropriation of Pfizer's proprietary data – which is not even occurring – when Pfizer itself has engaged in precisely the conduct it complains of by relying upon Sandoz's proprietary, draft protocol and

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Quality Of Medicines, European Pharmacopoeia Commission, PA/PH/Exp. 6/T (03) 43 ANP, Group Of Experts No. 6 (Biological Substances), Somatropin, Monograph N°: 951 (Dec. 2003), attached as Ex. 14; European Directorate For The Quality Of Medicines, European Pharmacopoeia Commission, PA/PH/Exp. 6/T (03) 44 ANP, Group Of Experts No. 6 (Biological Substances), Somatropin For Injection, Monograph N°: 952 (Dec. 2003), attached as Ex. 15; USP, 25 *Pharmacopeial Forum* 8540-8552 (July-Aug. 1999), In-Process Revisions for Somatropin and Somatropin for Injection, attached as Ex. 16; USP, 29 *Pharmacopeial Forum* 1978-1984 (Nov.-Dec. 2003), In-Process Revisions for Somatropin and Somatropin for Injection, attached as Ex. 17.

[12] As reflected throughout its petition, Pfizer proceeded to attempt to utilize Sandoz's Paragraph IV Patent Certification to support its petition. As the Agency knows from its ongoing review of Sandoz's confidential NDA, Sandoz's Patent Certification does not provide a scintilla of support for Pfizer's arguments.

[13] The disingenuous nature of Pfizer's current position is reflected in its prior demands that FDA protect its patent and non-patent exclusivity statutory benefits in the context of the 505(b)(2) regulatory regime FDA has been implementing for the past 20 years. See infra notes 22-25 and accompanying text.

placing that valuable commercial document on the public record in this proceeding, thereby depriving Sandoz of the value embodied in that study protocol.

The Contentions Advanced By Pfizer To Block Legitimate Competition Lack Merit

I. Pfizer's Unclean Hands Warrant Denial Of The Petition Because Pfizer, In Violation Of Its Own Corporate Policies, Has Put Another Company's Protocol On The Public Record And Thereby Engaged In An Even More Egregious Form Of The Conduct It Avowedly Seeks To Prevent FDA From Exhibiting

The value to a biopharmaceutical company of the details and design of its clinical trial protocols is beyond reasonable dispute. Companies like Sandoz, and even Pfizer, expend tens and sometimes hundreds of thousands of dollars to develop and refine clinical trial protocols to support development and ultimately regulatory approval of their products. The utility of a protocol lies not only in its pivotal role for the sponsor in the drug development process but also in its value to competitors who, with access to the protocol, no longer need to expend any resources (time or money) to complete clinical study design and can "free ride" on their competitor's work to glide to the market much more quickly than otherwise would have been the case.

The principles regarding the confidential and proprietary nature of the industry's study protocols have long been recognized by FDA, the courts, the industry, and even by Pfizer itself.

For its part, the Agency appropriately maintains a protocol as confidential until FDA has acted upon the application it supports. Thus, for example, 21 C.F.R. § 814.9(f)(2) provides:

> "(f) After FDA issues an order approving, or an order denying approval of any PMA, the following data and information in the PMA file are immediately available for public disclosure: . . . (2) Any protocol for a test or study unless the protocol is shown to constitute trade secret or confidential commercial or financial information under Sec. 20.61."

Similarly, when the courts have confronted efforts to have FDA release protocols for investigational products, the competitive harm of such disclosure has been reaffirmed. See Public Citizen Health Research Group v. FDA, 964 F.Supp. 413, 415 (D.D.C. 1997) (a claim of competitive harm could arise from disclosure of a protocol because it would provide "insight" into pre-approval test results and future marketing strategies), attached as Ex. 18.

Not surprisingly, FDA's longstanding position and the affirmation of that position by the courts have been advanced by the biopharmaceutical industry's very vocal stance regarding the proprietary and valuable nature of study protocols. One of the strongest, industry-wide proponents in this regard has been the Biotechnology Industry Organization ("BIO"), where

Pfizer has used its Board seat to very aggressively seek (and, on June 16th, secure) support for its petition despite eminently reasonable process and substantive issues raised by the scientists at a Sandoz sister company.[14]

Thus, in the one unique situation in which FDA proposed requiring sponsors to disclose, inter alia, "the protocols that outline how they expect to pursue each indication," BIO noted: "Individual sponsors may, in the past, have chosen to share such information through the NIH process and other public outlets. It is, however, still material that has long been considered confidential and protectable by the pharmaceutical and biotechnology industries." Comments of the Biotechnology Industry Organization Re: Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation (April 18, 2001), attached as Ex. 20. Indeed, in that same context, BIO highlighted the value of conducting clinical trials outside of the NIH process because of the protection afforded study protocols: "In short, some companies have the option of protecting all of their confidential commercial and trade secret information by proceeding outside the scope of NIH. FDA's Proposal, however, seeks to require disclosure even for those who have taken specific steps to protect their information." Id. (noting that some "companies provide gene therapy protocols; informed consent documents; and brief summaries of safety, efficacy and manufacturing information in response to the questions contained in the existing NIH Guidelines").[15]

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[14] See Steve Usdin, *Breaking Ranks*, 12 BioCentury A1-A3 (June 21, 2004), attached as Ex. 19.

[15] See also Comments of the Biotechnology Industry Organization Re: Recombinant DNA Research, Proposed Actions Under the NIH Guidelines (Feb. 12, 2001), attached as Ex. 21:

> Similarly, the information in an annual report would be of tremendous value to a competitor in the early stages of developing a competing product. A competitor could combine dose response information, preliminary effectiveness reports, and preclinical study results (submitted to NIH before the trial commences) to design a study specifically to demonstrate the superiority of its competing drug. (Ordinarily, a competitor would not have enough information to tailor its investigational plan in this manner.) Dose response information could tell the competitor which dose levels work and which do not. Dose response information combined with adverse event reports might show the maximum tolerable dose. The number of patients completing the trial, and the number of patients that have dropped out, could indicate if there was a problem with the study design, protocol requirements, dose, testing, or logistics. The previous year's clinical and non-clinical investigations could give a competitor an inside view of a company's development plan and perhaps even insight as to the specific animal models being developed for preclinical work. Some of this information could suggest agreements a company has with FDA. Protocol amendments to expand patient cohorts, or the addition of preclinical studies, could tell a competitor whether a company has made process changes. In short, disclosure of the information in an adverse event report and an annual report could allow a competitor to duplicate a company's work without the same expenditure of time and money, or even allow it to avoid expensive and time-consuming research altogether. The reports are therefore within [FOIA] Exemption 4.

The petitioner here, Pfizer itself, also has recognized the valuable and proprietary nature of study protocols, and has even gone so far as to adopt corporate policies to protect them. Most notable among these is Pfizer's Publication Policy:

> If requested by a medical journal when reviewing a submitted manuscript for publication, Pfizer will provide via the author, a synopsis of the clinical trial protocol and/or pre-specified plan for data analysis with the understanding that such documents are confidential and should be returned to Pfizer.

Policy on Public Disclosure of Clinical Trial Results, Section 3.1. Communication of Results by Pfizer, attached as Ex. 23. Pfizer's recognition of the confidential nature of clinical trial protocols is significant in light of Pfizer's corporate standards of conduct:

> Pfizer Policies on Business Ethics and Conduct
>
> All our employees, including our Chief Executive Officer, Chief Financial Officer and Principal Accounting Officer, ("Officers") are required to abide by our long-standing Standards of Business Ethics and Conduct to insure that our business is conducted in a consistently legal and ethical manner. These Standards form the foundation of a comprehensive process that includes compliance with all corporate policies and procedures, an open relationship among colleagues that contributes to good business conduct, and an abiding belief in the integrity of our employees. Our policies and procedures cover all areas of professional conduct, including employment policies, conflicts of interest, intellectual property and the protection of confidential information, as well as strict adherence to all laws and regulations applicable to the conduct of our business.

Pfizer Inc., Notice of Annual Meeting of Shareholders and Proxy Statement (March 17, 2003) at 9, attached as Ex. 24.[16]

Despite its own corporate policies and its own recognition of the inherently confidential nature of and value in clinical trial protocols, Pfizer has taken the unprecedented step of filing on the public record in this proceeding a competitor's clinical trial protocol. Pfizer's petition

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16 See also Pfizer Code of Business Conduct and Ethics for Directors, attached as Ex. 25:

> CONFIDENTIALITY
> Directors must maintain the confidentiality of information entrusted to them by the Company and any other confidential information about the Company that comes to them, from whatever source, in their capacity as a director, except when disclosure is authorized or legally mandated. For purposes of this Code, "confidential information" includes all non-public information relating to the Company.

assiduously avoids *any* statement as to either the circumstances regarding its acquisition, or the source, of the Sandoz protocol it obtained and publicly disclosed. (Sandoz has no information on the means by which Pfizer came into possession of Sandoz's valuable and proprietary internal draft protocol, which Pfizer unilaterally placed into the public record of these proceedings, thereby depriving Sandoz of its investment in the valuable business information set forth in that corporate document.) Pfizer's silence illuminates Pfizer's feet of clay even before its army of lawyers scurries to cobble together the predictable post hoc rationalization of Pfizer's conduct that undoubtedly will appear in a defensive filing for this proceeding.

In its petition, Pfizer asserts, erroneously, that FDA will engage in a similar type of conduct through "reliance on or through use of [Pfizer's] proprietary data". See, e.g., CP1 at 6. Notably, Pfizer does not suggest that FDA will disclose its proprietary data. Indeed, Pfizer cannot advance such an untenable assertion because FDA simply does not engage in that type of conduct as the Agency's Chief Counsel, Mr. Daniel Troy, reaffirmed during testimony on June 23rd before the U.S. Senate Judiciary Committee. Regrettably, Pfizer does.

"'It is one of the fundamental principles upon which equity jurisprudence is founded, that before a complainant can have a standing in court he must first show that not only has he a good and meritorious cause of action, but he must come into court with clean hands.'" Keystone Driller Co. v. General Elevator Co., 290 U.S. 240, 244 (1955) (quoting Story's Equity Jurisprudence, 14th ed., § 98). Pfizer lacks both. The governing principle of the unclean hands doctrine is "'that whenever a party who, as *actor*, seeks to set the judicial machinery in motion and obtain some remedy, has violated conscience, or good faith, or other equitable principle, in his prior conduct, then the doors of the court will be shut against him *in limine*; the court will refuse to interfere on his behalf, to acknowledge his right, or to award him any remedy.'" Id. at 244-45 (quoting Pomeroy, Equity Jurisprudence, 4th ed., § 397) (italics in the original). Accordingly, the doctrine of unclean hands is applied, in cases such as this one, "where some unconscionable act of one coming for relief has immediate and necessary relation to the equity that he seeks in respect of the matter in litigation." Id. at 245.

In the context of Pfizer's petition, there is an unambiguous nexus between Pfizer's deliberate act of putting Sandoz's draft protocol on the public record of this proceeding, and the relief Pfizer currently is seeking from FDA and that Pfizer undoubtedly will be seeking from the courts. See CP1 at 2 n.3. That clear connection should guide FDA, and ultimately will guide the courts, to apply the doctrine of unclean hands and deny Pfizer the relief it seeks in its petition. Keystone Driller, 290 U.S. at 245 (noting that courts "apply the maxim requiring clean hands only where some unconscionable act of one coming for relief has immediate and necessary relation to the equity that he seeks in respect of the matter in litigation").

II. Pfizer's Unclean Hands In Placing Sandoz's Internal Draft Protocol On The Public Record Has Produced The Conspicuous "Fruit Of The Poisonous Tree" – Unchecked And Fatal Reliance On A Glaring Typographical Error In Sandoz's Protocol

If the Agency is not inclined to deny the petition on the basis of Pfizer's unclean hands, denial is plainly warranted based upon the fruit of Pfizer's conduct: Pfizer's unreasonable reliance on a glaring typographical error in Sandoz's draft protocol.

As indicated at the outset, the crux of Pfizer's petition is that Omnitrope and Genotropin are "too different" because they allegedly "have chemically different active ingredients" based upon an asserted 1,001-daltons difference in their molecular weight. See, e.g., CP1 at 8. As FDA knows from its ongoing review of Sandoz's confidential NDA, these allegations are patently false. It also is glaringly obvious that this objectively and scientifically baseless allegation is the Achilles Heel of Pfizer's petition.

The average weight of an amino acid is approximately 135 daltons.[17] Pfizer grounds its case in an asserted 1,001 daltons difference between Genotropin and Omnitrope. If true, which it is not, such a massive difference in molecular weight would result in approximately a 7 amino acid difference between the active ingredients. The rhGH products currently marketed in the U.S. contain 191 amino acids – not 184 amino acids. In its petition, even Pfizer refers to 191 amino acids at least once. See CP1 at 4. Pfizer's petition would have been completely unnecessary if Omnitrope consisted of 184 amino acids, because the Agency properly would have refused to file an NDA. The Agency's ongoing, legitimate scientific review of the Omnitrope NDA demonstrates that the pivotal argument on which Pfizer's entire scientific case rests is without merit.[18]

Significantly, FDA imposes an affirmative obligation that requires an appropriate investigation into this key factual predicate of the petition:

> Currently, Sec. 10.30(b) requires a petitioner to certify, to its best knowledge and belief, that the petition includes all information and views on which the petitioner

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[17] See, e.g., Molecular Expressions: The Amino Acid Collection, Florida State University, National High Magnetic Field Laboratory (last modified Feb. 26, 2004), available at http://microscopy.fsu.edu/aminoacids/ (last accessed June 24, 2004).

[18] See 64 Fed. Reg. 66822, 66823-24 (Nov. 30, 1999) ("Although the existing regulation requires petitioners to provide a full statement of the factual grounds on which the petitioner relies, some petitions contain little or no evidence or support or rely on obsolete, irrelevant, or erroneous information. Thus, the proposal would deter the submission of frivolous or unsupported petitions and petitions which simply disagree with an agency decision regardless of the scientific evidence or legal authority supporting that decision, the importance of the public health policies supporting that decision, or the petitioner's lack of sound scientific evidence or legal authority to support its request.")

> relies and includes "representative data and information known to the petitioner which are unfavorable to the petition."

64 Fed. Reg. at 66824.[19] Again, Sandoz does not know the route by which Pfizer came to its "knowledge" of the typo in Sandoz's draft protocol. What is clear, however, is that Pfizer did not contact Sandoz to notify Sandoz that Pfizer had acquired the protocol or even to confirm the truth of its assertion regarding the molecular weight of Omnitrope. Under the circumstances, this is indefensible. By assuming that the draft protocol, however obtained, was perfect in every regard, Pfizer and its army of lawyers failed to fulfill their duty to pursue even a superficial and preliminary knowledge, let alone "best" knowledge, of the data on which their petition relies. As a result, they have submitted a petition that lacks a factual predicate and scientific credibility. On this basis alone, FDA should promptly deny the petition.

III. Pfizer's Attempt To Relitigate Once Again Its Position On Section 505(b)(2) Does Not Merit The Agency's Consideration – Particularly In The Face Of Pfizer's Documented Prior Acceptance Of FDA's Longstanding Policy On 505(b)(2) NDAs

Pfizer's legal arguments are as lacking in merit as its scientific arguments. From a legal perspective, Pfizer's petition boils down to the same, stale invective that Pfizer already has presented to the Agency on numerous other occasions over the last few years, and which the Agency appropriately has rejected. Although Pfizer's latest attempt to relitigate the same issue seeks to recast the argument in terms that Pfizer alleges are unique to recombinant FD&C Act drugs such as rhGH, a careful examination of Pfizer's contentions and of the statute reveals that Pfizer has not presented a legal issue warranting reconsideration of or a change in the Agency's longstanding and recently reaffirmed policy in this area.

Section 505(b)(2) was codified in 1984 as part of the Drug Price Competition and Patent Term Restoration Act of 1984 ("the Hatch-Waxman Amendments"). As Mr. Troy confirmed during his June 23rd testimony before the Senate Judiciary Committee, Section 505(b)(2) applies to FD&C Act products like rhGH approved pursuant to the Section 505 pathway. By its plain terms, Section 505(b)(2) provides:

> An application [may be] submitted under [section 505(b)(1)] for which the [safety and effectiveness] investigations . . . relied upon by the applicant [to support] approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person

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[19] See id. ("FDA is proposing to revise the certification statement. The proposed revision would have petitioners certify that, to the petitioner's best knowledge and belief, its citizen petition "includes all information and views on which the petition relies, that it is well grounded in fact and is warranted by existing laws or regulations, that it is not submitted for any improper purpose, such as to harass or to cause unnecessary delay, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.").

> by or for whom the investigations were conducted [and] shall also include [patent certifications for patents on the drug for which investigations were conducted or a method of use statement].

21 U.S.C. § 355(b)(2). Less than a year after Congress enacted the Hatch-Waxman Amendments, the Agency opened a public docket and requested comments on its implementation of this groundbreaking statute. 50 Fed. Reg. 21460 (May 24, 1985), attached as Ex. 26.[20] Although Pfizer had every opportunity to present its 505(b)(2) contentions to FDA in the context of that docket, it failed to do so.

Just two years later, in the first of many post-enactment open letters to the drug industry in 1987, written by Dr. Paul D. Parkman, then-Acting Director of the Center for Drugs and Biologics (the "1987 Parkman letter"), attached as Ex. 28, the Agency addressed the statutory 505(b)(2) pathway for approval of "modifications in approved drugs when such modifications require submission of clinical data." Id. at 1. Consistent with its longstanding and current approach to Section 505(b)(2), the Agency rejected the notion that a full NDA was required for such modifications because it would unnecessarily duplicate the basic safety and efficacy research that already had been completed. Instead, the Agency set forth what has been its consistent policy over the past 20 years: permitting a 505(b)(2) applicant to rely on the Agency's prior approval of a drug "to the extent that such reliance would be allowed under section 505(j) to establish the safety and effectiveness of the underlying drug." Id. As the Agency reaffirmed in its recent summary of Dr. Parkman's letter:

> Similarly, when reviewing a 505(b)(2) application that relies in part on the earlier approval of a listed drug, FDA may rely on its earlier conclusions regarding safety and effectiveness to whatever extent the conclusions are appropriate for the drug under review in the 505(b)(2) application. Although reliance on an FDA finding of safety and effectiveness for an NDA is certainly indirect reliance on the data submitted in the original NDA, reliance on the conclusions supported by that data is not the same as manipulating those data to reach new conclusions not evident from the existing approval.[21]

Again, in 1987, Pfizer had ample opportunity to object to this consistently applied interpretation of Section 505(b)(2), and once again they did not break their silence or expend any effort to protect their rights.

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[20] See also 50 Fed. Reg. 31887 (Aug. 7, 1985) (reopening of comment period), attached as Ex. 27.

[21] FDA Consolidated Response To Pfizer et al. Petitions, FDA Docket Nos. 2001P-0323/CP1 & C5, 2002P-0447/CP1, and 2003P-0408/CP1 at 10 n.14 (hereinafter "Pfizer Petition Denial"), attached as Ex. 29.

Two years later, based upon the comments the Agency had received during the preceding four-year period post-enactment, see 50 Fed. Reg. 21460, FDA initiated notice-and-comment rulemaking by promulgating a Proposed Rule implementing Hatch-Waxman. 54 Fed. Reg. 28872 (July 10, 1989). In that rulemaking, the Agency once again unambiguously set forth and further explained its longstanding and consistent interpretation of Section 505(b)(2):

> In addition to applications supported by literature reports or a combination of literature reports and new clinical investigations, FDA is proposing to treat as a 505(b)(2) application an application for a change in an already approved drug *supported by a combination of literature or new clinical investigations and the agency's finding that a previously approved drug is safe and effective.* . . . [T]hese applications will rely on the approval of the listed [previously approved] drug together with the data needed to support the change. *The applicant will thus be relying on the approval of the listed drug only to the extent that such reliance would be allowed under section 505(j) of the act: to establish the safety and effectiveness of the underlying drug.*

54 Fed. Reg. at 28891, 28892 (emphasis added).

Once again, Pfizer in 1989 was presented with an opportunity to comment on FDA's longstanding interpretation of Section 505(b)(2). Finally, in response to that 1989 Proposed Rule, Pfizer took the opportunity to present its position and submitted voluminous, comprehensive comments to the Agency regarding FDA's proposed implementation of Hatch-Waxman, including FDA's policy on Section 505(b)(2) NDAs.[22] Significantly, contrary to the position Pfizer repeatedly has been attempting to stake out for the past four years, Pfizer not only failed to challenge FDA's consistent interpretation of the statute, but Pfizer accepted FDA's 505(b)(2) policy, noting that the 505(b)(2) NDA pathway was one of "two separate, non-overlapping categories of *less-than-full applications*." Id. at 22 (emphasis added).[23]

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[22] FDA Docket No. 85N-0214, Vol. 1, C21, Letter From James C. Shehan, Pfizer, to Dockets Management Branch (HFA-305) (Jan. 8, 1990) at 21-22, attached as Ex. 30.

[23] Pfizer's only substantive comment on FDA's regulatory implementation of Section 505(b)(2) addressed NDAs that otherwise could be submitted as ANDAs preceded by public ANDA Suitability Petitions. Id. at 21-22. During the intervening three years between the 1989 proposal and 1992 finalization of the Agency's notice-and-comment rulemaking, that very transparent, public process only produced "two comments on the proposed provisions regarding 505(b)(2) applications, neither of which addressed FDA's fundamental interpretation of section 505(b)(2). These comments were addressed in the preamble of the final rule that established the regulation at § 314.54 governing the types of applications that could be submitted under section 505(b)(2)." Pfizer Petition Denial at 11-12 (citing 57 Fed. Reg. 17950 at 17954 (April 28, 1992)).

More importantly, after submitting its public comments to the rulemaking docket, Pfizer submitted a then-non-public (but subsequently docketed) letter to the Agency,[24] which presented exactly the same interpretation of Section 505(b)(2) as that which FDA has applied consistently for the past 20 years:

> In addition, in the case of section 505(b), if an application is not required to contain the same data as a previous, full application, the reason why must be that *the second applicant is relying explicitly or implicitly on studies performed by or for someone other than the applicant – studies that either generate "paper" contained in the second application or that are relied on more generally by the applicant and FDA reviewers to conclude that a particular scientific or medical question has been answered sufficiently to dispense with the need for relevant evidence in the application, despite the fact that the first applicant was required to submit evidence to answer the question. In that case, the second application is properly considered under section 505(b)(2), so that the applicant under section 505(b)(1) receives the benefit of the patent notification and exclusivity provisions applicable to paper NDAs.* . . . First, if a subsequent applicant is excused from submitting an original investigation to answer a question deemed relevant by Center reviewers for the first applicant, the subsequent applicant is necessarily relying on investigations that were not conducted by or for that applicant. That reliance occurs despite the fact that the investigations that answer the question – or even the need for them – may have become obscured by the passage of time. *We believe that reliance on such investigations, although indirect or tacit, is functionally equivalent to direct reliance on published studies in the form of a traditional "paper NDA" and should give rise to the same result, i.e., submission and review under section 505(b)(2).*

Id. at 4-5 (emphasis added) (underscoring in the original). See id. at 5 ("The second reason why an NDA lacking the same investigations that were required in a pioneer NDA must be reviewed under section 505(b)(2) is that failure to do so implicates the constitutional and statutory rights of holders of pioneer NDAs").[25]

In sum, 14 years ago, Pfizer willingly accepted FDA's longstanding interpretation and application of Section 505(b)(2). Indeed, as indicated by the following analysis, there is no

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[24] Letter From Marvin R. Frank, Pharm.D., J.D., Pfizer, To Mr. Gerald F. Meyer, FDA (June 5, 1990), accompanying RC1, FDA Docket No. 93P-0115 (April 22, 1993), filed in FDA Docket No. 85N-0214 (May 26, 1993), attached as Ex. 31.

[25] Significantly, in this context, Pfizer was attempting to protect its statutory benefits under Section 505(b)(2) and was demanding that FDA preclude subsequent applicants from avoiding the statutory patent and exclusivity provisions of Section 505(b)(2) by filing a Section 505(b)(1) NDA. See id. at 4 ("That issue concerns the extent to which an applicant seeking a second or subsequent approval for a drug product under section 505(b)(1) is required to meet the same data requirements that were imposed on the first successful applicant").

meaningful distinction between Pfizer's "legacy" position in 1990 as documented above and the Agency's consistent application of its policy in this area.

As the Agency indicated in 1989, a fundamental premise of Section 505(b)(2) – and the "linchpin of FDA's interpretation of 505(b)(2)," Pfizer Petition Denial at 14 – is that a sponsor can rely upon FDA's prior determination or "finding" that a previously approved drug cited in the 505(b)(2) NDA is safe and effective. That longstanding and consistently applied policy was reaffirmed last October by the Agency, when it appropriately and forcefully rejected Pfizer's prior attempt to block 505(b)(2) NDA approvals:

> [T]he 505(b)(2) application can rely on the finding of safety and effectiveness of the listed drug only to the extent the product seeking approval and the listed drug are the same. To the extent the products are different, the 505(b)(2) application, like a stand alone NDA, must include sufficient data to demonstrate that the product with those different aspects meets the statutory approval standard for safety and effectiveness.

Pfizer Petition Denial at 3. The Agency's longstanding and consistent intention in permitting reliance on the prior safety and efficacy determination is straightforward: it permits the "industry to rely to the greatest extent possible under the law [and to the extent such reliance is scientifically justified] on what is already known about a drug" in order "to avoid requiring drug sponsors to conduct and submit studies that are not scientifically necessary." Id. As FDA succinctly put it last October: "The conduct and review of duplicative studies would (1) divert industry resources that could be used to undertake innovative research, (2) increase drug costs, (3) strain FDA review resources, and (4) slow the process for drug approval with no corresponding benefit to public health. In addition, the conduct of duplicative studies raises ethical concerns because it could subject human beings and animals to medically or scientifically unjustified testing." Id. at 3-4.

As highlighted by FDA in rejecting Pfizer's arguments previously, the 505(b)(2) NDA process has been utilized extensively on an industry-wide basis. See id. at 19-21. Following FDA's prior decision, in preparation of this submission, an inventory of all 505(b)(2) NDAs has been compiled based upon publicly-available approval records on CDER's website, which reflects the overwhelming, industry-wide reliance on FDA's longstanding and consistent application of the statute over the past 20 years. See 505(b)(2) NDA Inventory, attached as Ex. 22.

In the context of Pfizer's latest regurgitation of its tired arguments, one of those (b)(2) NDA approvals stands out: the Agency's June 22, 1998, approval of Novo Nordisk's 505(b)(2) NDA for GlucaGen (glucagon [rDNA origin] for injection). See FDA Approval Letter, attached as Ex. 32. The GlucaGen 505(b)(2) administrative precedent involving a recombinant drug is significant in two respects. First, it demonstrates the fallacy in Pfizer's contention that the

Omnitrope NDA and its review by the Agency is in some way precedent-setting.[26] As indicated by NovoNordisk's own 505(b)(2) NDA for a recombinant product, the Omnitrope application is nothing more than a continuation of the Agency's longstanding policy in this area. This conclusion is reinforced by the Agency's judicially-confirmed approval of a Section 505(j) ANDA for a menotropins product derived from mammalian urine.[27]

Second, and at least as important, it establishes that FDA had approved a 505(b)(2) NDA for a therapeutic protein drug product prior to the issuance of the Agency's Draft Guidance for Industry: Applications Covered by Section 505(b)(2), FDA Docket No. 99D-4809 (Oct. 1999), attached as Ex. 34. In the face of Pfizer's continuing assaults on the Agency, this is significant because it was only in 2000 – 16 years after enactment of Hatch-Waxman and 13 years after FDA first publicly stated its interpretation of the statute – that Pfizer attempted to cast off the laches that had arisen from its demonstrable record of assent to FDA's interpretation of 505(b)(2). In 2000, working with the same outside law firm that filed the instant petition, Pfizer advanced the same legal arguments that it once again is attempting to relitigate in this proceeding. See FDA Docket No. 99D-4809, C1 (Feb. 7, 2000) (Fax Message From Kathleen M. Sanzo to FDA Dockets Management Branch), attached as Ex. 35. No matter how many times Pfizer continues repeating the mantra set forth in that laggard submission from 2000, see CP1 at 2 n.3, Pfizer cannot at this late hour undo its own silence or upend FDA's 20-year track record of consistent application and interpretation of Section 505(b)(2).

If Pfizer wants relief at this juncture, there is only one forum in which its complaints should be heard: the U.S. Congress. In fact, after the Agency last fall issued a well-reasoned, 35-page opinion denying Pfizer's last petition, Congress took up and enacted a variety of amendments to Section 505(b)(2).[28] As a matter of statutory construction and administrative law, it is well settled that knowledge of the statutory interpretations and regulatory decisions taken by regulatory agencies such as FDA is imputed to Congress.[29] Consequently, applying principles of ratification, Congress is legally presumed to have knowledge of, and to have ratified, FDA's 505(b)(2) interpretation – as set forth in both the rulemaking proceedings over the past 20 years

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[26] It has been suggested in the context of the brewing debate on follow-on biologics that the first precedent in this area actually involved a biologics license application for a Public Health Service Act-regulated product. See Berlex Laboratories, Inc. v. FDA, 942 F. Supp. 19 (D.D.C. 1996). Obviously, analysis of such products is beyond the scope of this proceeding.

[27] See Serono Laboratories, Inc. v. Shalala, 158 F.3d 1313 (D.C. Cir. 1998), attached as Ex. 33. The lead, Pfizer in-house lawyer on the instant petition is very familiar with that case, as he was lead counsel in the District Court defending FDA's approval of the generic menotropins product in that case.

[28] Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Pub. Law No. 108-173, Title XI, Subtitle A, Sec. 1101(b). See also Act Nov. 21, 1997, P.L. 105-115, Title I, Subtitle B, § 125(d)(2)(B).

[29] "Congress is presumed to be aware of an administrative or judicial interpretation of the statute . . . ." Lorillard v. Pons, 434 U.S. 575, 580 (1978).

and in FDA's denial of Pfizer's last petition. Putting aside that legal presumption, Pfizer had ample opportunity to petition Congress last year to change the law during Congress' deliberations on other amendments to Section 505(b)(2). Once again, however, Pfizer was mute and sat on its rights.

In the face of Pfizer's silence (and that of the rest of the innovator industry), Congress proceeded to amend Section 505(b)(2) substantially – without in any way amending FDA's 20-year application of the statute. Congress' failure to overturn FDA's longstanding regulations at the end of 2003, like its failure to amend Section 505(b)(2) to change FDA's interpretation at any other point over the past 20 years, provides the most direct, concrete evidence of the validity of FDA's lawful interpretation and application of the statute.[30]

At this juncture, FDA does not need to do anything more than transmit a simple, one-page denial letter to Pfizer, attaching yet another copy of the Agency's reasoned, 35-page opinion rendered just last year.

CONCLUSION

Pfizer has not provided a cognizable reason for FDA to alter course from the well-trodden path so well delineated in the Agency's rejection of Pfizer's last petition. To the contrary, the invalidity of Pfizer's contentions reinforces both the importance and necessity for the Agency to continue and complete its confidential scientific review of Sandoz's confidential NDA. Sandoz is confident that FDA's scientists can complete their diligent expert reviews of Sandoz's proprietary data and render an appropriate decision with respect to authorizing the lawful marketing of Omnitrope.

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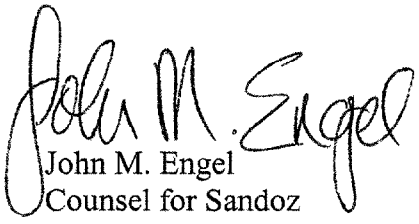
[30] "It is settled law that when a statute has an authoritative interpretation, and Congress reenacts it without change, 'Congress is presumed to be aware of [the] interpretation . . . and to adopt that interpretation. . . .'" In Re: Armitage Fee Application, 50 F.3d 42, 45 (D. C. Cir. 1995) (quoting Lorillard, 434 U.S. at 580).

Accordingly, for all of the foregoing reasons, the Agency should summarily deny Pfizer's petition.

Respectfully submitted,



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Opposition To Pfizer Petition Seeking To Block FDA's Lawful Approval Of Omnitrope®
Docket No. 2004P-0231/CP1

Table Of Exhibits

1. Pfizer, Inc., Exhibit for 10K for Fiscal Year 2003, U.S. SEC (filed March 10, 2004), Exhibit 13, 2003 Financial Report at 50

2. Genentech v. Bowen, 676 F. Supp. 301 (D.D.C. 1987)

3. Genentech v. Novo Nordisk A/S, 108 F.3d 1361 (Fed. Cir. 1997), cert. denied, 522 U.S. 963 (1997)

4. Novo Nordisk A/S et al. v. Bio-Technology General Corp., Ltd., et al., 2003 U.S. Dist. LEXIS 10098 (D. Del., June 9, 2003)

5. *Pharmacia Genotropin Human Growth Hormone Launch Set For Early 1996*, F-D-C Reports, The Pink Sheet, 57(36):(Sept. 4, 1995), at T&G-10

6. *Bio-Technology General Bio-Tropin Preliminary Injunction Upheld*, F-D-C Reports, The Pink Sheet, 58(16):(April 15, 1996), T&G-3-T&G-4

7. *Serono Saizen Human Growth Hormone Approved With Three-Times Weekly Dosing Schedule; Somatropin Product Labeling Carries Hypothyroidism Precaution*, F-D-C Reports, The Pink Sheet, 58(42):(October 14, 1996), at 6

8. Pharmacia & Upjohn, Inc., Pre-Effective Amendment No. 2 to Form S-4, As Filed With The Securities And Exchange Commission on September 15, 1995, at 136

9. *Generic Somatropin NDAs Would Require Human Immunogenicity Tests – FDA*, F-D-C Reports, The Pink Sheet, 64(16): (April 22, 2002), at 14

10. European Pharmacopoeia at 1940-1942, Somatropin Bulk Solution Monograph No. 01/2002:0950

11. European Pharmacopoeia at 1937-1939, Somatropin Monograph No. 01/2002:0951

12. European Pharmacopoeia at 1942-1944, Somatropin for Injection Monograph No. 01/2002:0952

13. European Directorate For The Quality Of Medicines, European Pharmacopoeia Commission, PA/PH/Exp. 6/T (03) 42 ANP, Group Of Experts No. 6 (Biological Substances), Somatropin bulk solution, Monograph N°: 950 (Dec. 2003)

14. European Directorate For The Quality Of Medicines, European Pharmacopoeia Commission, PA/PH/Exp. 6/T (03) 43 ANP, Group Of Experts No. 6 (Biological Substances), Somatropin, Monograph N°: 951 (Dec. 2003)

15. European Directorate For The Quality Of Medicines, European Pharmacopoeia Commission, PA/PH/Exp. 6/T (03) 44 ANP, Group Of Experts No. 6 (Biological Substances), Somatropin for Injection, Monograph N°: 952 (Dec. 2003)

16. USP, 25 *Pharmacopeial* Forum 8540-8552 (July-Aug. 1999), In-Process Revisions for Somatropin and Somatropin for Injection

17. USP, 29 *Pharmacopeial* Forum 1978-1984 (Nov.-Dec. 2003), In-Process Revisions for Somatropin and Somatropin for Injection.

18. Public Citizen Health Research Group v. FDA, 964 F. Supp. 413, 415 (D.D.C. 1997).

19. Steve Usdin, *Breaking Ranks*, 12 BioCentury A1-A3 (June 21, 2004).

20. Comments of the Biotechnology Industry Organization Re: Availability for Public Disclosure and Submission to FDA for Public Disclosure of Certain Data and Information Related to Human Gene Therapy or Xenotransplantation (April 18, 2001).

21. Comments of the Biotechnology Industry Organization Re: Recombinant DNA Research, Proposed Actions Under the NIH Guidelines (Feb. 12, 2001).

22. 505(b)(2) NDA Inventory

23. Pfizer, Inc., Policy on Public Disclosure of Clinical Trial Results, Section 3.1. Communication of Results by Pfizer

24. Pfizer Inc., Notice of Annual Meeting of Shareholders and Proxy Statement (Mar. 17, 2003).

25. Pfizer Code of Business Conduct and Ethics for Directors.

26. 50 Fed. Reg. 21460 (May 24, 1985)

27. 50 Fed. Reg. 31887 (Aug. 7, 1985)

28. Letter to the Drug Industry by Dr. Paul D. Parkman, then-Acting Director of the Center for Drugs and Biologics (1987)

29. FDA Consolidated Response to Pfizer et al. Petitions, FDA Docket Nos. 2001P-O323/CP1 & C5, 2002P-O447/CP1, and 2003P-O408/CP1

30. FDA Docket No. 85N-0214, Vol. 1, C21, Letter from James C. Shehan, Pfizer, to Dockets Management Branch (HFA-305) (Jan. 8, 1990) at 21-22

31. Letter from Marvin R. Frank, Pharm.D., J.D., Pfizer, to Mr. Gerald F. Meyer, FDA (June 5, 1990), accompanying RC1, FDA Docket No. 93P-0115 (April 22, 1993), filed in FDA Docket No. 85N-0214 (May 26, 1993)

32. FDA Approval Letter for Novo Nordisk's GlucaGen (glucagon [rDNA origin] for injection) (June 22, 1998)

33. Serono Laboratories, Inc. v. Shalala, 158 F.3d 1313 (D.C. Cir. 1998)

34. Draft Guidance for Industry: Applications Covered by Section 505(b)(2), FDA Docket No. 99D-4809 (Oct. 1999)

35. FDA Docket No. 99D-4809, C1 (Feb. 7, 2000) (Fax Message from Kathleen M. Sanzo to FDA Dockets Management Branch)